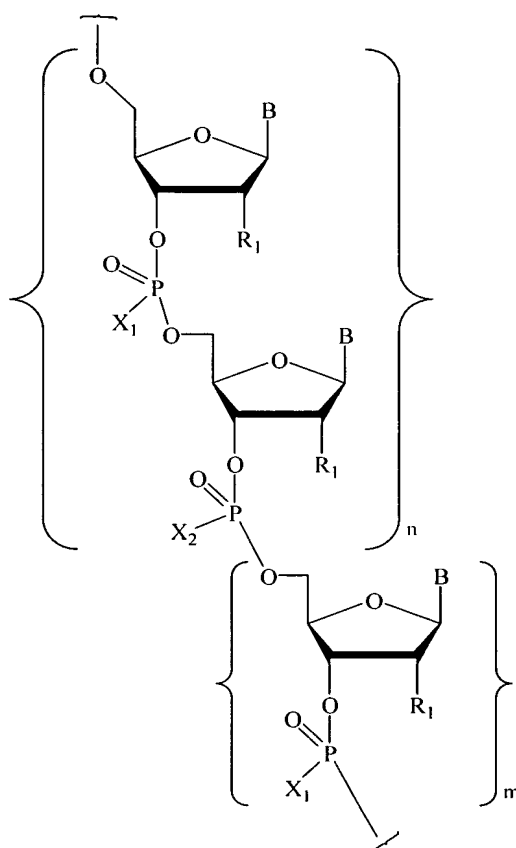


This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1-27. (Canceled).

28. (Currently amended) A method for reducing the undesired production of a protein in an organism, said method comprising contacting an said organism with a compound of formula:



wherein:

each B is a nucleobase;

one of X_1 or X_2 is O , and the other of X_1 or X_2 is S ;

each R_1 , is, independently, H , hydroxyl, C_1 - C_{20} alkyl, C_3 - C_{20} alkenyl, C_2 - C_{20} alkynyl, halogen, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O -alkyl, S -alkyl, NH -alkyl, N -dialkyl, O -aryl, S -aryl, NH -aryl, O -aralkyl, S -aralkyl, NH -aralkyl, amino, N -phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato,

sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, or polyether;

or R₁ is a group of formula Z-R₂₂-(R₂₃)_v;

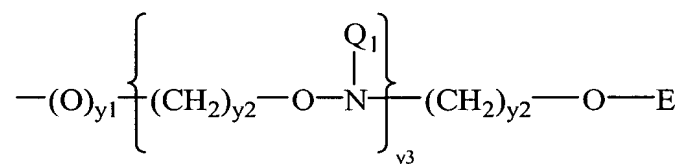
Z is O, S, NH, or N-R₂₂-(R₂₃)_v;

R₂₂ is C₁-C₂₀ alkyl, C₂-C₂₀ alkenyl, or C₂-C₂₀ alkynyl;

R₂₃ is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, or polyether;

v is from 0 to about 10;

or R₁ has the formula:



wherein:

y₁ is 0 or 1;

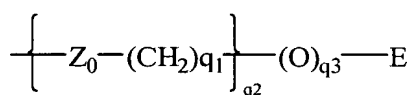
y₂ is independently 0 to 10;

y₃ is 1 to 10;

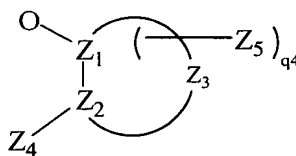
E is C₁-C₁₀ alkyl, N(Q₁)(Q₂) or N=C(Q₁)(Q₂);

each Q₁ and Q₂ is, independently, H, C₁-C₁₀ alkyl, substituted alkyl, dialkylaminoalkyl, a nitrogen protecting group, a tethered or untethered conjugate group, a linker to a solid support; or Q₁ and Q₂, together, are joined in a nitrogen protecting group or a ring structure that can include at least one additional heteroatom selected from N and O;

or R₁ has one of formula I or II:



I



II

wherein:

Z_0 is O, S, or NH;

q^1 is from 0 to 10;

q^2 is from 1 to 10;

q^3 is 0 or 1;

q^4 is, 0, 1 or 2;

Z_4 is OM_1 , SM_1 , or $N(M_1)_2$;

each M_1 is, independently, H, C_1 - C_8 alkyl, C_1 - C_8 haloalkyl, $C(=NH)N(H)M_2$, $C(=O)N(H)M_2$ or $OC(=O)N(H)M_2$;

M_2 is H or C_1 - C_8 alkyl;

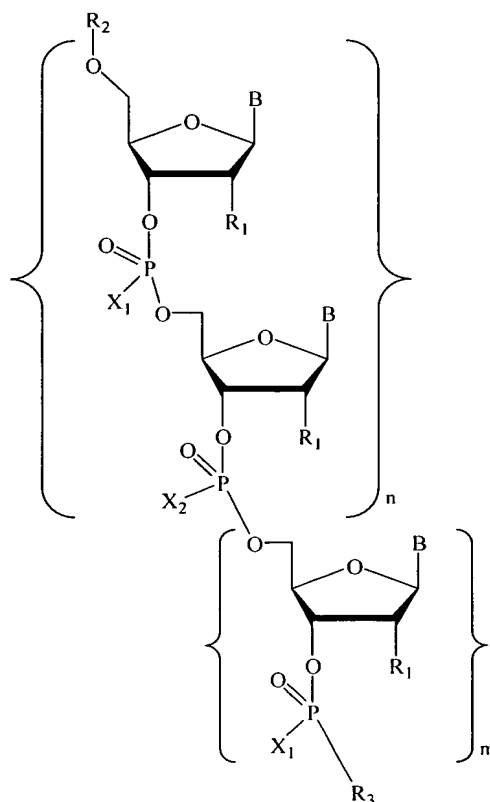
Z_1 , Z_2 and Z_3 comprise a ring system having from about 4 to about 7 carbon atoms, or having from about 3 to about 6 carbon atoms and 1 or 2 hetero atoms wherein said hetero atoms are selected from oxygen, nitrogen and sulfur, and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic; and

Z_5 is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms, $N(Q_1)(Q_2)$, OQ_1 , halo, SQ_1 or CN;

n is from 2 to 50; and

m is 0 or 1.

29. (Currently amended) A method for reducing the undesired production of a protein in an organism, said method comprising contacting ~~an~~ said organism with a compound of formula:



wherein:

each B is a nucleobase;

X_1 is S;

X_2 is O;

each R_1 , is, independently, H, hydroxyl, C_1 - C_{20} alkyl, C_3 - C_{20} alkenyl, C_2 - C_{20} alkynyl, halogen, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, or polyether;

or R_1 is a group of formula $Z-R_{22}-(R_{23})_v$;

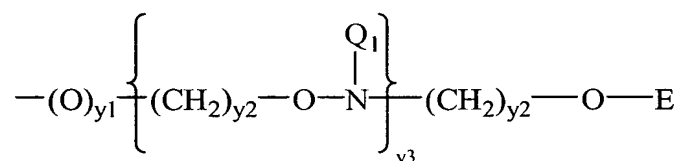
Z is O, S, NH, or $N-R_{22}-(R_{23})_v$;

R_{22} is C_1 - C_{20} alkyl, C_2 - C_{20} alkenyl, or C_2 - C_{20} alkynyl;

R₂₃ is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, or polyether;

v is from 0 to about 10;

or R₁ has the formula:



y₁ is 0 or 1;

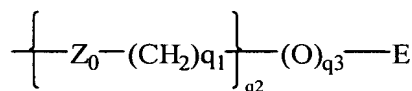
y₂ is independently 0 to 10;

y₃ is 1 to 10;

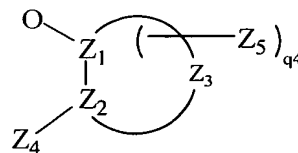
E is C₁-C₁₀ alkyl, N(Q₁)(Q₂) or N=C(Q₁)(Q₂);

each Q₁ and Q₂ is, independently, H, C₁-C₁₀ alkyl, substituted alkyl, dialkylaminoalkyl, a nitrogen protecting group, a tethered or untethered conjugate group, a linker to a solid support; or Q₁ and Q₂, together, are joined in a nitrogen protecting group or a ring structure that can include at least one additional heteroatom selected from N and O;

or R₁ has one of formula I or II:



I



II

wherein:

Z₀ is O, S, or NH;

q¹ is from 0 to 10;

q² is from 1 to 10;

q^3 is 0 or 1;

q^4 is, 0, 1 or 2;

Z_4 is OM_1 , SM_1 , or $N(M_1)_2$;

each M_1 is, independently, H, C_1 - C_8 alkyl, C_1 - C_8 haloalkyl, $C(=NH)N(H)M_2$, $C(=O)N(H)M_2$ or $OC(=O)N(H)M_2$;

M_2 is H or C_1 - C_8 alkyl;

Z_1 , Z_2 and Z_3 comprise a ring system having from about 4 to about 7 carbon atoms, or having from about 3 to about 6 carbon atoms and 1 or 2 hetero atoms wherein said hetero atoms are selected from oxygen, nitrogen and sulfur, and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic; and

Z_5 is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms, $N(Q_1)(Q_2)$, OQ_1 , halo, SQ_1 or CN ;

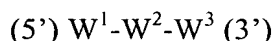
n is from 2 to 50; and

m is 0 or 1;

R_2 is H, a hydroxyl protecting group, or an oligonucleotide; and

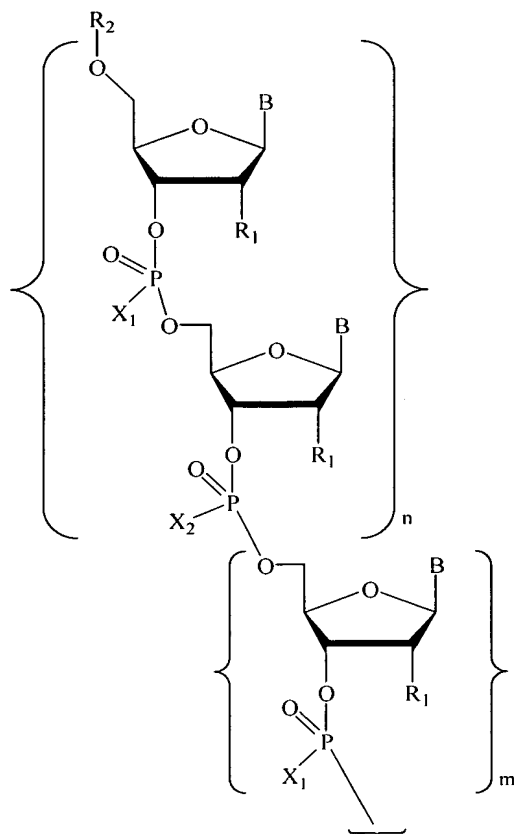
R_3 is OH, an oligonucleotide, or a linker connected to a solid support.

30. (Currently amended) A method for reducing the undesired production of a protein in an organism, said method comprising contacting ~~an~~ said organism with a compound of formula:



wherein:

W^1 has the Formula:



wherein:

each B is a nucleobase;

one of X₁ or X₂ is O, and the other of X₁ or X₂ is S;

each R₁, is, independently, H, hydroxyl, C₁-C₂₀ alkyl, C₃-C₂₀ alkenyl, C₂-C₂₀ alkynyl, halogen, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, or polyether;

or R₁ is a group of formula Z-R₂₂-(R₂₃)_v;

Z is O, S, NH, or N-R₂₂-(R₂₃)_v;

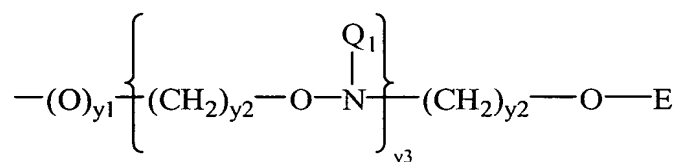
R₂₂ is C₁-C₂₀ alkyl, C₂-C₂₀ alkenyl, or C₂-C₂₀ alkynyl;

R₂₃ is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-

aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, or polyether;

v is from 0 to about 10;

or R₁ has the formula:



y₁ is 0 or 1;

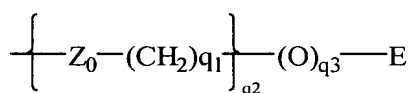
y₂ is independently 0 to 10;

y₃ is 1 to 10;

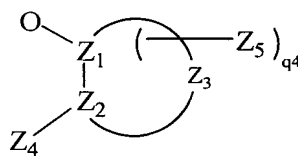
E is C₁-C₁₀ alkyl, N(Q₁)(Q₂) or N=C(Q₁)(Q₂);

each Q₁ and Q₂ is, independently, H, C₁-C₁₀ alkyl, substituted alkyl, dialkylaminoalkyl, a nitrogen protecting group, a tethered or untethered conjugate group, a linker to a solid support; or Q₁ and Q₂, together, are joined in a nitrogen protecting group or a ring structure that can include at least one additional heteroatom selected from N and O;

or R₁ has one of formula I or II:



I



II

wherein:

Z₀ is O, S, or NH;

q¹ is from 0 to 10;

q² is from 1 to 10;

q³ is 0 or 1;

q⁴ is, 0, 1 or 2;

Z_4 is OM_1 , SM_1 , or $N(M_1)_2$;

each M_1 is, independently, H, C_1 - C_8 alkyl, C_1 - C_8 haloalkyl, $C(=NH)N(H)M_2$, $C(=O)N(H)M_2$ or $OC(=O)N(H)M_2$;

M_2 is H or C_1 - C_8 alkyl;

Z_1 , Z_2 and Z_3 comprise a ring system having from about 4 to about 7 carbon atoms, or having from about 3 to about 6 carbon atoms and 1 or 2 hetero atoms wherein said hetero atoms are selected from oxygen, nitrogen and sulfur, and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic; and

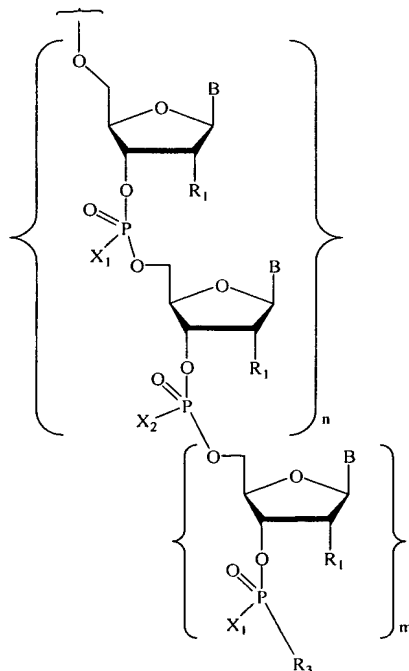
Z_5 is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms, $N(Q_1)(Q_2)$, OQ_1 , halo, SQ_1 or CN;

n is from 2 to 50; and

m is 0 or 1;

R_2 is H, a hydroxyl protecting group, or an oligonucleotide;

W^3 has the Formula:



wherein R_3 is OH, an oligonucleotide, or a linker connected to a solid support; and

W² is a plurality of covalently bound nucleosides linked by phosphodiester or phosphorothioate linkages.

31-51. (Canceled).

52. (Previously presented) The method of claim 28 wherein R₁ is -O-CH₂-CH₂-O-CH₃.

53. (Previously presented) The method of claim 28 wherein n is about 5 to about 50.

54. (Previously presented) The method of claim 28 wherein n is about 8 to about 30.

55. (Previously presented) The method of claim 28 wherein n is about 4 to about 15.

56. (Previously presented) The method of claim 28 wherein n is 2 to about 10.

57. (Previously presented) The method of claim 29 wherein R₁ is -O-CH₂-CH₂-O-CH₃.

58. (Previously presented) The method of claim 29 wherein R₂ is H, and R₃ is OH.

59. (Previously presented) The method of claim 29 wherein R₂ is a phosphodiester-linked oligonucleotide or a phosphorothioate linked oligonucleotide.

60. (Previously presented) The method of claim 29 wherein R₃ is a phosphodiester-linked oligonucleotide or a phosphorothioate linked oligonucleotide.

61. (Previously presented) The method of claim 29 R₂ and R₃ are each a phosphodiester-linked oligonucleotide or a phosphorothioate linked oligonucleotide.

62. (Previously presented) The method of claim 30 wherein R₁ is -O-CH₂-CH₂-O-CH₃.

63. (Previously presented) The method of claim 30 wherein R_2 is H, and R_3 is OH.
64. (Previously presented) The method of claim 30 wherein n is about 5 to about 50.
65. (Previously presented) The method of claim 30 wherein n is about 8 to about 30.
66. (Previously presented) The method of claim 30 wherein n is about 4 to about 15.
67. (Previously presented) The method of claim 30 wherein n is 2 to about 10.
68. (Previously presented) The method of claim 30 wherein W^2 is a plurality of covalently bound nucleosides linked by phosphodiester linkages.
69. (Previously presented) The method of claim 30 wherein W^2 is a plurality of covalently bound nucleosides linked by phosphorothioate linkages.